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The ultimate goal of this project is to combine features derived from ultrasound (US) images, US radio-frequency (RF) data, tissue elasticity imaging, and clinical data such as PSA into a computerized system for displaying prostate images that indicate probable location(s) of cancer. This project proposed to begin by gathering RF data from in-vitro prostatectomy specimens in cross sectional planes 2mm apart. These data are used to calculate RF features such as scatterer size, and backscatter coefficient at each location in the gland. The data are also used to generate images and elastograms from which image texture features and tissue hardness features are computed. The features are then correlated with histology taken at the same tissue planes to determine which features and feature combinations most accurately predict the presence of cancer.

Despite continuing delays in hiring personnel to do work on the project, considerable progress in development of the ultrasound signal processing algorithms has been made. We have developed a user interface for the software, and have developed algorithms to calculate RF and statistical texture features for the data. In addition, collection of clinical data has continued with 79 prostate glands having been examined producing perhaps the largest database ever of complete prostate histology with ultrasound correlation. Slow progress on the assembly of quarter sections into whole mount sections for comparison with the ultrasound images has been achieved because no person to do the work was found. The work of assembling the images will now be performed by the research assistant supervised by the PI with the Department of Pathology in a consultative role.

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Brian K Garner
(electronic signature) 28 Dec 2000

PI - Signature Date

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INTRODUCTION

The ultimate goal of this project is to combine features derived from ultrasound (US) images, US radio frequency (RF) data, tissue elasticity imaging, and clinical data such as PSA into a computerized system for displaying prostate images that indicate probable location(s) of cancer. Each of these different classes of features has been shown to be useful for prostate cancer detection. By combining those features in each class that perform best in a set of test cases, we hope to develop an accurate tool for detecting regions on the ultrasound image that a high probability for cancer. Eventually we hope these techniques will be used to rapidly identify high probability areas and mark them on the ultrasound image in real time or near real time.

This project began by gathering RF data from in-vitro prostatectomy specimens in cross sectional planes 2mm apart using a linear array transducer. These data are used to calculate RF features such as power spectrum slope, and backscatter coefficient at each location in the gland. The data are also used to generate images and elastograms from which image texture features and tissue hardness features are computed. The features will be correlated with histology taken at the same tissue planes to determine which features and feature combinations most accurately predict the presence of cancer. The various image, hardness, and RF features will then be combined with prior probability information derived from an AFIP 3D model of prostate occurrence and with clinical PSA values to produce a system that can accurately identify the presence of prostate cancer using ultrasound data.

After developing the techniques to perform identification of prostate cancer using the linear array scans, our plan is to migrate the technique to data from a curved array transducer and then finally to data from an endorectal prostate probe. We hope in the end to be able to demonstrate an in vitro system using an endorectal prostate probe that will be able to mark areas of high probability for cancer on each ultrasound image. This will prepare us for an in vivo study directed at developing an ultrasound system that can better direct biopsies of the prostate gland to areas of high likelihood for actual prostate cancer.

RESEARCH ACTIVITIES AND PROGRESS

Administrative Overview:

Our efforts in the second year of the project have been focused on continuing the clinical data acquisition begun in June 1999, working with the new graduate student on the development of software to compute the ultrasound based features, and working with the department of pathology on the development of methods to reassemble the light microscopic images into whole mount equivalents that can be directly compared with the ultrasound data being collected.

The graduate student, scheduled to arrive in January 2000, did not actually arrive until late April 2000 due to difficulties obtaining a proper Visa to work in the United States. In May and June 2000, training of the student in the techniques and theory needed for the project was undertaken but was hampered by language difficulties that were more severe than anticipated. Most of the remainder of the summer was spent allowing the student to adjust to the language and to gain familiarity with Matlab programming concepts. The training process continued in September with a training trip to the FDA in Rockville Maryland. Now, the graduate student, Mr. He, is becoming proficient and is able to develop the code needed to do the ultrasound signal processing with close supervision by the PI.

The Department of Pathology at the University of Vermont had agreed to take an active role in assembling the pathology slide images – an operation that originally was to be performed at George Washington University. The department did assign the project to a pathology resident, but over time it was clear that she did not the have the time to complete the review and assembly of the pathology images into a 3-D database as we had originally intended. In meetings with Pathology and the cell biology lab, I proposed that they hire additional help to be funded from the contract. After several months however, it was clear that they were not going to be successful at finding additional help. At this point, I decided to add the pathology image assembly process to the duties of my research assistant, a physician from Bosnia, increasing her hours from half to full time. This necessitated a change in the position description – a process that has been underway for the past two months. In the meantime, additional equipment needed to convert microscope slides to digital images has been procured and the research assistant has been trained in the use of the equipment.

In summary, because of lack of personnel willing or able to work on the project, progress has been slow—especially in areas that were to be supervised by persons other than the PI. We are on track with respect to clinical data acquisition having made up six months of lost time at the start of the project, but are behind in assembly and analysis of the pathology data being generated by Dr. Trainer. We are still far behind in the ultrasound data analysis but are catching up now that Mr. He is beyond his training phase. I have requested a no cost extension to finish the work of the project and will be getting heavily involved in the details of pathology image assembly and ultrasound data analysis to get those components back on track for completion.

RESEARCH PROGRESS

Task 1 (Months 1-6): Collect RF data on 25 prostate glands with the linear array transducer. Develop a preliminary plan for data acquisition for tasks 5 and 7.

This portion of the project was completed prior to the last annual report and is outlined in that document. No further changes to data acquisition were made in the past year other than a reduction in the number of sutures used to mark the index slice of the ultrasound study. This change was done to reduce the amount of time that the specimen spent in the ultrasound lab prior to being received by pathology.

Task 2 (months 1-6): Develop a methodology for registering optical pathology information with ultrasound data.

The procedure for registration of pathology information with ultrasound data has been refined since the prior report. The process of taking pathology data and matching it to the corresponding ultrasound image and location involves several steps. The prostatectomy specimen is fixed in buffered formalin after the ultrasound scan is complete. This process stiffens the tissue so that less deformation occurs during sectioning. Then the surface of the gland is marked with inks of various colors. The gland is then sliced into multiple transverse sections with the plane of the sections being perpendicular to the posterior surface of the gland. This is simply achieved by placing the posterior surface down on the cutting table and cutting downward vertically.

After the transverse sections are made in pathology, each section is further divided into quarters to that the tissue will fit on a standard microscope slide. The pathologist examines the section quarters and all foci of cancer are marked on the glass slide with indelible ink. Then the slides (quarter sections) are digitized for reassembly into complete sections (also known as "whole mount" sections). After several attempts at using photomicrography to digitize the sections, a simpler alternative was found to work quite well. The glass slides are simply arranged on the tray of a transparency flatbed scanner and "scanned" in at a resolution of 200-400 dpi. This resolution provides more than enough detail to identify all cancer locations marked with ink without generating unreasonably large file sizes. The digitized images are then placed into Adobe Photoshop, and the images are "warped" slightly to fit better with each other. This is necessary since some shrinkage and distortion occurs during the sectioning and fixation process. We also use this same software to make the microscope images match even more closely to the ultrasound images. This is done on the assembled histologic cross section by simply adjusting the shape of the histologic image of the gland to match the ultrasound image shape. No fiducial markers are being used since all of the candidates for marker materials would interfere with the sectioning of the gland or with microscope slide preparation.

Initially, our plan for registering the prostate data with pathology data called for defining the first image of the prostate by sewing silk or prolene suture into the capsule of the prostate at four locations along the plane of the first slice. These sutures would then be used to line up the plane of the first scan so that it would be perpendicular to the long axis of the gland and would

also be used by the pathologists to locate the position of their first slice through the gland. In practice, the procedure proved to be too cumbersome and time consuming to allow us to promptly scan the glands. Instead, one or two sutures are sewn into the capsule near the apex of the gland. Then the gland is carefully lined up in the water tank so that the scan planes are perpendicular to the long axis of the gland. The scan containing an image of the sutures is identified (typically the second or third slice) and is used to correlate slice position with pathology. For example, slice three on the ultrasound may contain the image of the suture whereas slice 2 of the pathology may contain the suture. In this situation, ultrasound slice 2 corresponds to pathology slice three. The other slices are related to each other by taking the ratio of the number of slices taken through the gland. For example, if 15 slices are taken using ultrasound and only 12 were taken in pathology, the spacing between slices is 2mm for ultrasound and 15/12 x 2mm = 2.5mm and ultrasound slices correspond to pathology according to the table 1 below:

Table 1: Example of ultrasound/pathology data correspondence (for case of 15 US slices and 12 pathology sections where sutures are seen in US slice 3 and path slice 2)

US Slice	Position in Gland (mm)	Corresponding Path Slice(s)
1	0	none
2	2	1 (1.5)
3	4	2
4	6	3 (6.5)
5	8	3-4 (6.5-9)
6	10	4-5 (9-11.5)
7	12	5 (11.5)
8	14	6
9	16	7 (16.5)
10	18	7-8 (16.5-19)
11	20	8-9 (19-21.5)
12	22	9 (21.5)
13	24	10
14	26	11 (26.5)
15	28	11-12 (26.5 – 29)

In the above example, pathology slices .5mm or closer to the ultrasound slice position are correlated alone with the ultrasound image whereas slices >.5mm away require examination of two adjacent pathology slices for correlation. In most cases, foci of prostatic cancer are large enough to appear on several consecutive slices making correlation of ultrasound data with pathology relatively straightforward.

Due to beamwidth considerations, the suture may be visible on two adjacent ultrasound slices. This introduces further uncertainty into the exact pathology slice with which the ultrasound data should be correlated. The solution to this problem is to only use cancer foci that are large enough to appear on several pathology slices. Then the ultrasound slices lying closest to the

center of the lesion at pathology are used to identify ultrasound data coming from a cancer. This reduces the possibility that ultrasound data coming from normal prostate tissue will be misclassified as cancerous during the classifier or neural network training process.

After matching histology and ultrasound "slices" the plan for finding the ultrasound RF data to be classed as "cancer" is this:

1. After the histologic sections have been reassembled with ink marks on cancer areas, match each section to the corresponding "slice" of ultrasound data.
2. Superimpose the histologic image on the ultrasound image or elastogram to confirm that the images match with respect to shape, rotation and size. Mark out the same region on the ultrasound image that corresponds to the location of cancer on the histologic image and process only that RF data for texture features and RF features. We have software under development that can do this.
3. Evaluate the RF and texture features for features that seem to discriminate between cancer and normal tissue.
4. The same process will be carried out on the elastographic strain images to determine if strain values are useful for cancer detection.
5. Normal areas of the glands will be used to gather data about the RF, Texture, and strain values of normal prostatic tissue.

Task 3 (months 1-6): Use digital database of prostate cancer rate developed at Georgetown University and AFIP to establish a probability map of prostate cancer in a 3D domain.

To reveal the spatial pattern of localized prostate cancer distribution, a three-dimensional (3-D) statistical volumetric model, showing the probability map of prostate cancer distribution together with the anatomical structure of the prostate, has been developed from 70 digitally imaged surgical specimens. Through an enhanced virtual environment with various visualization capabilities, this master model permits for the first time an accurate characterization and understanding of prostate cancer distribution patterns. The construction of the statistical volumetric model is characterized by mapping all of the individual models onto a generic prostate site model, in which a self-organizing scheme is used to decompose a group of contours

representing multifold tumors into localized tumor elements. A crucial step in creating the master model is the development of an accurate multi-object and non-rigid registration/warping scheme incorporating various variations among these individual models in true 3-D. This is achieved with a multi-object based principle-axis alignment and an affine transform, and followed by a thin-plate spline interpolation driven by the surface based deformable warping dynamics. Based on the accurately mapped tumor distribution, a standard finite normal mixture is used to model the cancer volumetric distribution statistics. The process is graphically outlined in Figure 3 below:

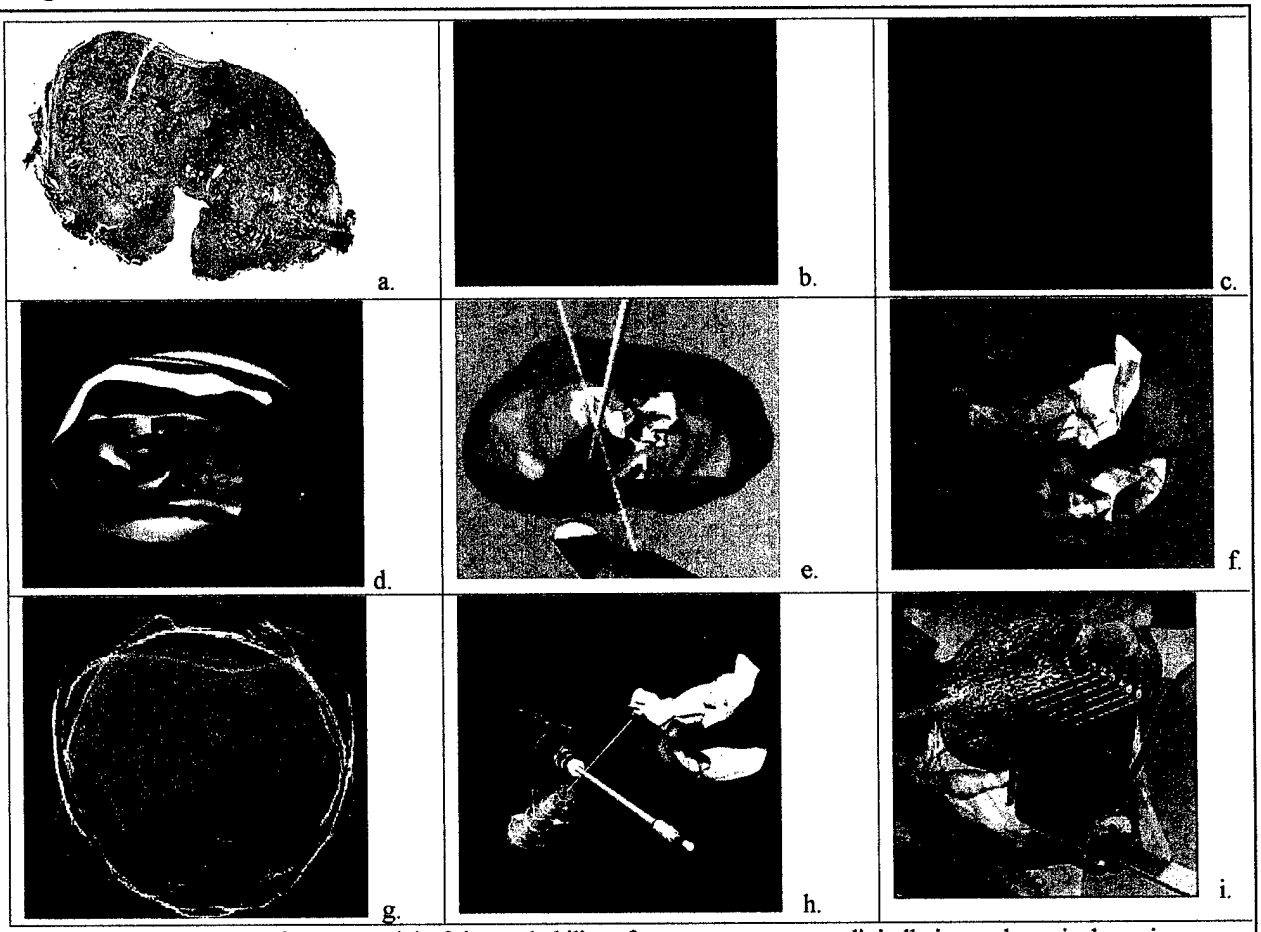


Figure 3. Development of a 3D model of the probability of prostate cancer. a. digitally imaged surgical specimens, b. decomposition of tumor contours, c. reconstruction of multifocal tumors, d. prostate site model in 3D computer graphics, e. TRUS based biopsy simulation virtual environment, f. display of multifocal tumor distribution, g. 3D statistical volumetric model of tumor spatial distribution -- data from this model will be used to calculate prior probabilities for the current study, h. biopsy planning, i. Model guided biopsy-- in our proposal actual ultrasound data with the added model data will be used.

The above has already been accomplished with the AFIP data. All that remains is to reconcile the alignment of the model and the sections or slices we obtain with the appropriate location in the model. This work has yet to be accomplished due to illness of Dr. Lo, the investigator responsible for this component. Also, since our database will be larger than the AFIP one used

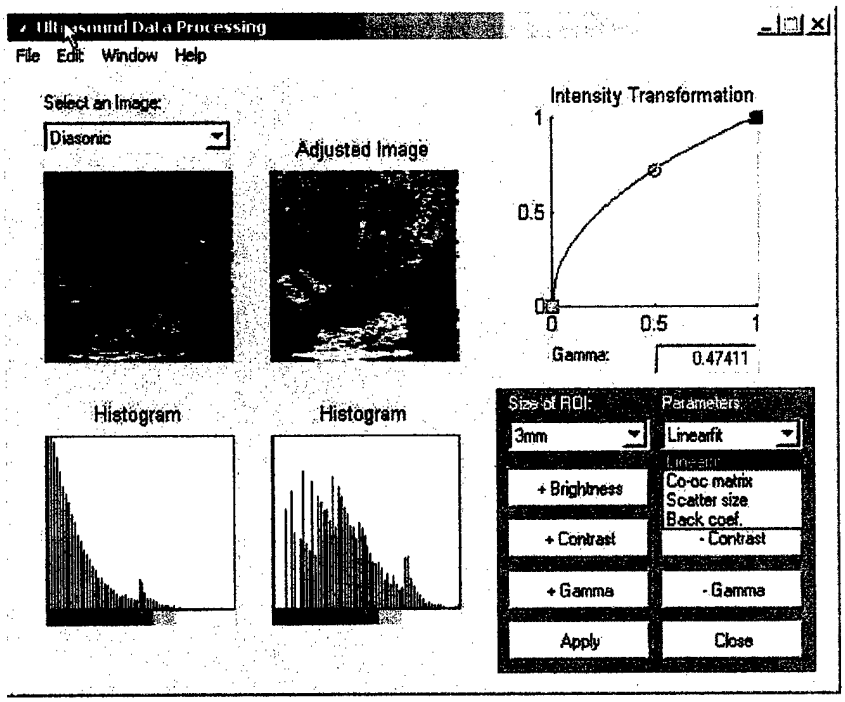
to create the model, we are looking into incorporating our data into the model to improve the cancer probability estimates.

Task 4 (months 1-9): Software development.

Overview and GUI

Development of software for computation of ultrasound based tissue features began with the arrival of Xhe He, a graduate student from mainland China in April 2000. Initially, time was spent familiarizing Mr. He with the basics of the project, MATLAB programming, and the programs previously written by Rash Mia. By June 2000, programs to read the Diasonics data, to display an image generated from RF data and to extract a subset of RF data for feature calculation had been developed. By October 2000, the original command driven programs and Dr. Wear's older graphical interface were replaced with a new graphical user interface that will allow less sophisticated users to process the ultrasound data (figure 3). The interface allows the user to adjust image quality and to select a region of interest for further processing to generate the RF based and texture features that will be used to help distinguish cancers from benign tissue. This version of the interface allows the user to generate a square ROI but future versions will allow for more flexibility in ROI generation. In the lower right, the user may select from a list of features to be calculated from the RF within the ROI. The plan is to locate cancers on ultrasound images by comparison with corresponding pathology slices, to select the region containing cancer using the interactive interface shown and then to calculate textural, RF and elastographic features for the cancer regions of interest.

Figure 3. Example of the graphical user interface to be used for prostate ultrasound data processing.



Selection of RF and Texture Features

Mr. He has been hampered by a lack of a strong background in image processing and ultrasound physics. This made it difficult for him to understand the procedures used in previously written software well enough to properly incorporate the routines into the integrated application needed for this project. To help resolve this situation, the PI accompanied Mr. He on a trip to Washington, D.C. in September 2000 for training sessions with Drs. Wagner and Wear of the FDA. Over two days, Mr. He received background training on ultrasound signal processing, RF tissue characterization features, texture-based features and on ROC analysis for classifier performance evaluation. Given the inexperience of Mr. He a new strategy for the development of an effective set of ultrasound based tissue characterization features was needed. It was decided to start by developing software for the computation of the following features—all of which have shown promise in the distinction of cancer from benign tissue:

1. Tissue ultrasound signal to noise ratio: μ/σ
2. Integrated backscatter coefficient
3. Slope of normalized backscatter intensity vs. frequency curve
4. Y intercept of the backscatter intensity vs. frequency curve

Feature 1 above may be useful because it may be another way to measure the relative contribution of specular vs. diffuse tissue backscatter components. These have been previously shown to be of value for characterization of both liver and kidney tissue[1,2].

Feature 2 is likely to be of value because it relates to the brightness visible on standard ultrasound images and prostatic cancers are well known to have a lower brightness than normal prostatic tissue.

Features 3 and 4 have been successfully used by Feleppa et.al.[3] for differentiation of prostatic cancer from benign tissue.

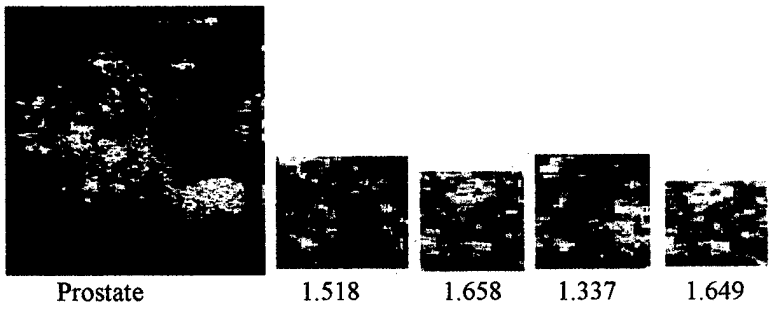
Code to calculate texture based features based on the co-occurrence matrix that have already proved valuable for prostatic cancer[4,5] has already been completed. Features that can be calculated include: Entropy, Contrast, ASM, and Correlation[6]. These features will be added to the four listed above if they prove useful for distinction of prostate cancer in this series.

Preliminary Tests of Feature Computation Software

Software development following the September meeting was directed at three goals:

1. Develop software to compute the four features above.
2. Test the software on phantoms and a small clinical data set.
3. Develop the user interface to allow either computation of features from a user-selected region of interest or automatically from multiple regions of interest over the entire RF data set.

By mid October 2000, progress in each of the four areas had been made. Figure 4 shows a typical prostate image generated from RF data plus the calculated signal to noise ratios for several regions of interest in the section.

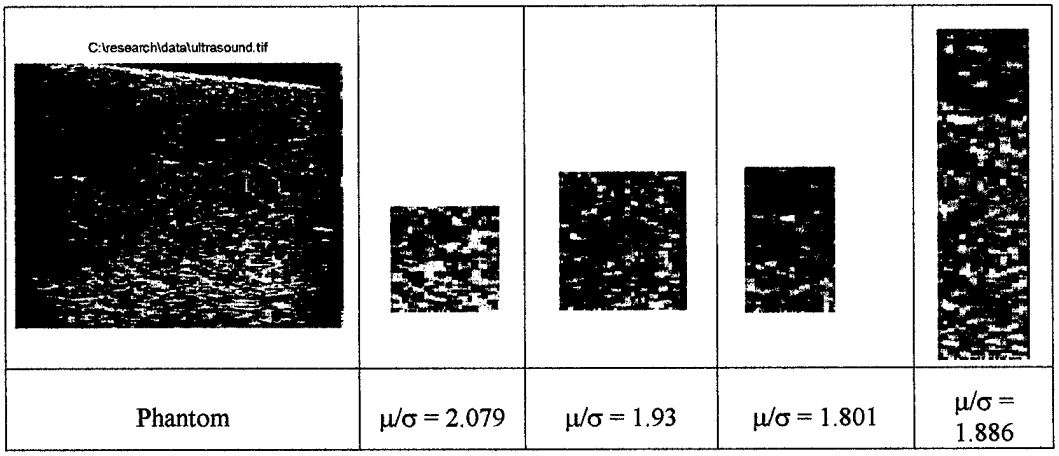


Prostate	1.518	1.658	1.337	1.649

Figure 4. Signal to Noise ratio (μ/σ) values for subregions of a prostate section (case 22).

The theoretical maximum value for an image with fully developed speckle is 1.91. For an image with specular as well as diffuse scatterers, the value will be lower. The subregions all have values less than 1.91—an indication that the subregions contain specular as well as diffuse, randomly positioned scatterers. This is an expected result since tissue rarely exhibits purely diffuse scattering. Other tested sections have yielded similar results.

Signal to noise ratios have also been calculated for our tissue mimicking phantom. This phantom has predominately small scatters and contains very few specular scatterers. It should therefore exhibit a μ/σ value very close to 1.91. Figure 5 below demonstrates that subregions calculated from within the phantom do in fact exhibit a μ/σ close to 1.91.



Phantom	$\mu/\sigma = 2.079$	$\mu/\sigma = 1.93$	$\mu/\sigma = 1.801$	$\mu/\sigma =$ 1.886

Figure 5. Tissue mimicking calibration phantom. Signal to noise ratio for four subregions of the phantom image. Average value for the four regions: 1.924.

Another feature that has been successfully computed is the slope of the backscatter vs. frequency plot. Figure 6 shows an example of this computation.

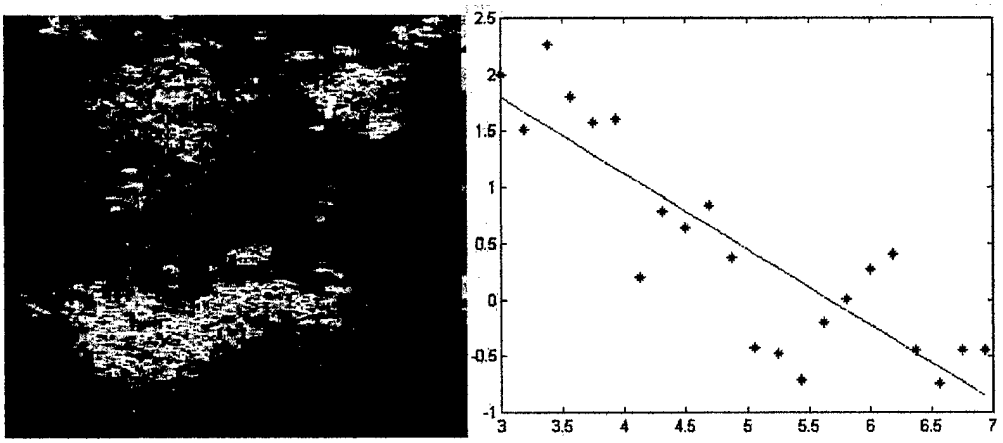


Figure 6. Plot of RF amplitude vs. frequency for a subregion of prostate tissue. The region of interest in the prostate image (left) was used to compute signal intensity vs. frequency (right) and a linear fit to the data.

As expected based on observations by Feleppa, the slope generally has a negative value. The example shown here does not include a correction for beam intensity profile, focusing, diffraction, and time gain compensation setting. Feleppa performed this correction by using a reflection from a flat glass plate immersed in water at the same depth as the data in the ROI. Instead of a glass plate, we use the scattering from a known tissue mimicking reference phantom for our calibration[7].

Figure 7. Linear reverberation artifact in phantom data

Using tissue mimicking phantom data does present some challenges though. The phantom data may contain reverberation artifacts caused by the acoustic impedance mismatch between the phantom surface and the surface of standoff pad attached to the transducer. These artifacts must be removed before using the phantom data to avoid using an improper correction on the patient data (figure 7). Software is being developed to search the phantom data for anomalous values that will then be removed and replaced with interpolated data. Since the phantom has a constant backscatter coefficient and well-defined attenuation properties, interpolation is an effective means of replacing artifacts with usable data for calibration.

In addition to development of algorithms for the computation of features from a user defined region of interest, some effort has been directed at developing software to automatically calculate features from multiple regions of interest over an entire RF data set (image) in order to produce a parametric image for each slice corresponding to the b-mode image. A preliminary

version of the software has been completed and some initial parametric images have been produced (figure 8).

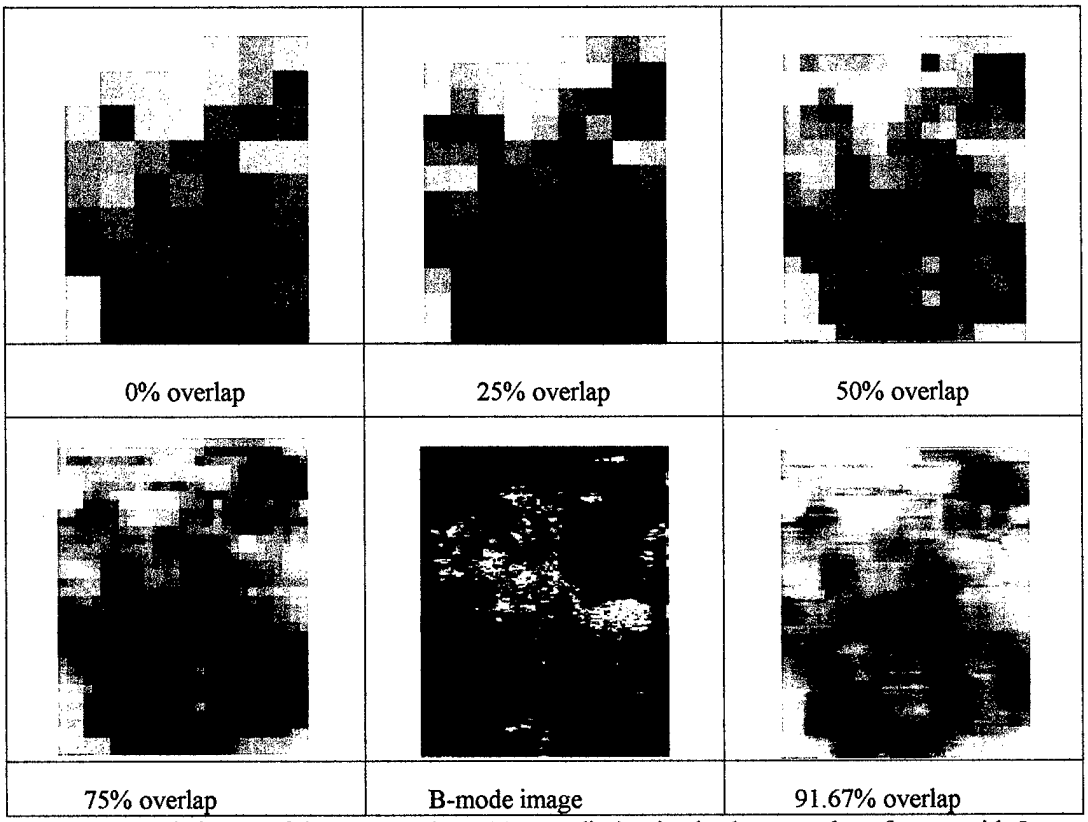
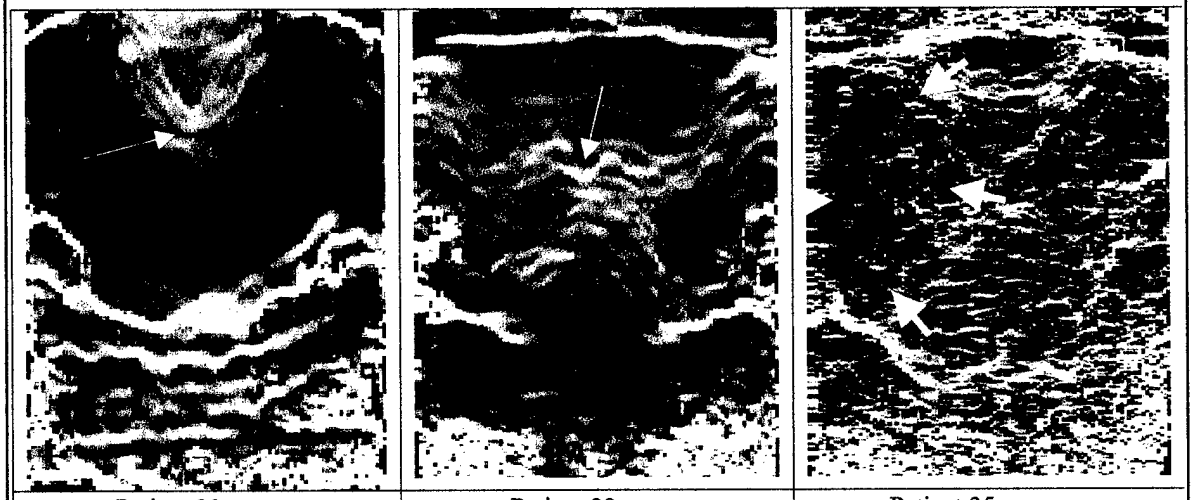


Figure 7. Parametric image of the prostate (case 22, one slice) using backscatter slope feature with 5mm x 12 RF vector regions of interest (ROI) with various degrees of overlap of the regions of interest. Greater apparent detail is evident in the images with greater ROI overlap. No resampling was performed to smooth out the pixellated appearance. In practice bicubic interpolation would be used to further smooth the image.

Relatively large subregions must be used to reduce the variance of the calculated slope values and use of overlapping regions is a method of increasing the apparent spatial resolution of the image when larger subregions are necessary. The images demonstrate the higher level of detail afforded by using overlapping subregions. We intend to display parametric images during the development process to confirm proper operation of the software but in the end, the parametric data sets will be combined with elastographic and clinical probability data to produce a single image in which overall probability of cancer (based on all features) is displayed for clinical use. It is likely that the experience we gain in producing these intermediate parametric images will help us to better display the final result—a parametric image where cancer probability is the parameter.

Elastography

The acquired data have been used to produce preliminary elastograms using axial elastogram software previously developed. Examples of elastograms are shown in figure 8.



Patient 20	Patient 29	Patient 35

Figure 8. Axial Elastograms of prostates of three different patients. Note the verumontanum seen well in two of the patients (arrows). The higher resolution apparent in the image from patient 35 is due to the use of greater overlap in the strain computation windows used to generate the elastogram. Note the area of apparent increased hardness (short arrows) on the right side suggestive of carcinoma. We have not generated high resolution elastograms on all cases yet, preferring to wait for newer software that provides

Axial elastograms are of limited quality because lateral strains not accounted for produce decorrelation and artifacts in the axial strain image (elastogram). Our plan is completely reprocess all data using new software that corrects for lateral strains to obtain higher quality strain data for correlation with the other RF based features. This software is being tested currently by our consultants at the University of Texas and hopefully will be ready by April 2001. In the meantime, we have had to consider the potential problem of how to normalize the data since differing amounts of stress (transducer displacement and pressure) may have been applied in each case. We believe that this will not be a big problem, but will attempt to estimate the amount of compression applied during elastogram generation by measuring the reduction in thickness of the gel pad standoff before and after the compression has been performed. The elastic modulus of the gel pad will be measured separately using standard methods and this will give us both the displacement used, and an estimate of the force applied. We may even be able to estimate axial elastic moduli within the image on a point-by-point basis. At the very least, we will have a calibration scheme to adjust strain values from each case to make them directly comparable to those from other cases.

Task 5 (months 12-18): Data Fusion

The appropriate path to proper data fusion is now clearer than it was a year ago. Once the normalized strain values are obtained from the elastogram, these can be combined with the results of the other features for the same location in each image using either statistical pattern recognition techniques or neural network methods. To ease the process of integration, the same

window sizes will be used to process the ultrasound data for different features wherever possible. If larger regions are needed for some features (such as image texture features), greater ROI overlap will be used to obtain the appropriate number of data points in each image or dataset. We have purchased some 3-D modeling software (Neuro Lucida) that will help us to truly integrate all of our 2-D data into a comprehensive 3-D data set that can be used visualization and for modeling of biopsy patterns. This will further increase the potential value of the data we have thus far acquired.

Task 6 (months 7-18): More prostate data collection.

Some initial experiments with larger compressions were completed, but as the software needed to process these data has not yet been received from the Univ. of Texas, the analysis of these data are as yet incomplete. Tests with a curved array prostate probe were not carried out because of this lack of software and failure of the scanner itself as noted below.

In mid October 2000 the Diasonics spectra system used to acquire digital RF data from prostate glands began experiencing intermittent boot failures and two weeks later, became inoperable. Although General Electric Corp. (who purchased Diasonics several years ago) has committed to providing service for the system, it is not clear that the expertise exists to repair a system that has been out of production for almost a decade. We are presently searching for persons who have experience on the system who might be able to attempt repairs but at this point, the chance of success is estimated to be <50%. If the system should prove irreparable, further data acquisition will be carried out with a new ATL 1000 system that should become usable for RF acquisition and elastography in mid February 2001. Some modifications to software will be necessary however since the data format is quite different. The ATL system will be used for experiments using curved arrays (tasks 6 and 8) that will take place after further analysis of the Diasonics data. New software that provides lateral motion correction and lateral elastography is scheduled to arrive in mid February along with the remaining hardware needed to make the ATL system operational for elastography.

Task 7 (months 11-22): Compute RF and texture features for all stage 1 acquisitions.

Work on task 7 will begin as soon as the feature computation software is complete—a process that will probably require another 2-4 months including time for coding the remaining features and for testing. The computation of features will be a rapid process but determination of the most discriminating features must await completion of the pathology analysis and matching of pathology to ultrasound data.

Task 8 and Task 9 (months 13-26 and 24-30): Acquire RF with a curved array transducer.

This is delayed until our results for the linear array are more complete. Due to the failure of the Diasonics scanner, the new ATL scanner with elastography capability will probably be used for this phase.

KEY RESEARCH ACCOMPLISHMENTS

- Developed software for automated computation of multiple features for multiple regions of interest across entire ultrasound images ("slices"). Some further refinement and automation is needed.
- Developed a reliable method for digitizing microscope slides from pathology. Also developed procedures for reassembling entire prostate cross-sections from quarter section images using Adobe Photoshop.
- Refined the method of registering ultrasound RF prostate cross-sections with cross-sectional images obtained in pathology. This system will allow correlation of ultrasound RF data with corresponding pathology with a spatial error of 2mm or less.
- Acquired a large set of pathology and ultrasound data from prostate glands containing cancer (79 cases to date). Acquisition halted pending further analysis of existing data and because of scanner failure.

REPORTABLE OUTCOMES

The sizeable database of completely sectioned prostate glands with complete pathology analysis and corresponding ultrasound images and raw US data is a valuable resource that may be useful to other researchers. Initially we plan to collaborate with AFIP to combine our data with theirs in a 3D model of prostatic carcinoma probability.

CONCLUSIONS

The project continues to be plagued by lack of personnel able to perform the required tasks. Despite this problem, we are making slow progress and have not discovered any fundamental flaw that would prevent us from eventually reaching our goals. As before, our goal is to provide clinicians with an ultrasound based tool that can direct them to areas with a high probability for cancer so that they can properly direct their transrectal biopsies.

It should be noted that although our in vitro project was supposed to provide a logical basis for in vivo trials, some in vivo data will likely become available before our study is complete. Specifically, a French group is acquiring in vivo prostate RF data in vivo as part of a study of cancer treatment using high intensity focused ultrasound. We may be able to use that data with our analysis methods to significantly speed up the introduction of our method into clinical practice.

We now have collected a large database of completely sectioned prostate glands containing cancer with correlative ultrasound data. With further analysis of the pathology, this will provide a resource for us and for others wishing to study the distribution of cancer in greater detail. 3-D modeling of the prostate gland using our histology data is being planned and should result in a

better understanding of the patterns of involvement of prostate cancer. It will also represent a valuable comparison with similar sized data set already assembled by the AFIP.

Although we are still playing "catch up" in the ultrasound data processing arena, we are now making steady progress and will have a unique multi-feature data set of complete prostate glands with complete histologic correlation quite soon.

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